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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,116	01/16/2001	Vedrana S. Susulic	0630/1E791-US1	3094

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EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	14

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,116	SUSULIC ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 4/14/03 as Paper No. 13, in which several claims were amended (claims 28, 33, 38, 39). Claims 28-39 are pending in the instant application.

Any rejection of record not addressed in the instant office action is hereby withdrawn. This action is not final due to new grounds of rejection made herein that were not necessitated by applicants' amendment of the claims in Paper No. 13.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection**.

Each of the rejected claims is directed towards a method for screening for a compound that increases or inhibits the activity of an Sp1 or B segment-binding B_3-AR *trans*-activating factor in human cells. A critical element of the invention is the Sp1 or B segment-binding B_3-AR *trans*-activating factor. As written, the claims encompass an Sp1 or B segment-binding B_3-AR *trans*-activating factor obtained from literally any source. Thus, the claims encompass a

very broad genus of such transcriptional factors that must transactivate expression of a B_3 adrenergic receptor in different mammalian systems (e.g. murine, canine, etc.). Additionally, the proteins must be predictive of how the human proteins in human cells will respond to a given test compound.

The instant specification describes the mammalian Sp1 and B segment-binding B_3-AR *trans*-activating factors by function only, with no real description as to what is the primary structure of the protein. Even for the Sp1 protein described by the instant specification, the description is only that it is "Sp1 like" due to its ability to bind a unique polynucleotide sequence in its role as activator of human B_3 adrenergic receptor expression. There is no basis for one of skill in the art to be able to envision a representative number of embodiments of the claimed trans-activation factors, even by function. As the specification teaches, there is a difference in the way that the murine and human homologs of the B_3 adrenergic receptor are expressed (e.g. tissue distribution).

Given that the claims encompass a broad genus of possible Sp1 and B segment-binding B_3-AR trans-activating factors that must be predictive of the human proteins, and given that the prior art and instant specification do not describe such proteins in such a way that the skilled artisan can envision the broadly claimed genus, much less those whose activity is predictive of the human proteins, the skilled artisan would not have been able to envision the broadly claimed genus of Sp1 and B segment-binding B_3-AR trans-activating factors embraced by the rejected claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention at the time of filing.

Claims 28-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments where the cells contacted in the assay actually produce the human Sp1 or B segment-binding B_3-AR *trans*-activating factor and wherein the contacted cells are actually human cells, does not reasonably provide enablement for embodiments where the cells do not actually produce the human Sp1 or B segment-binding B_3-AR *trans*-activating factor or where the assay cells are not human cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. **This is a new rejection.**

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The invention is drawn to a series of assays for screening for a compound that increases or inhibits the activity of an Sp1 or B segment-binding B_3-AR *trans*-activating factor. The invention is complex in that it is directed to screening for compounds that affect the level of expression or activity of a pair of transcriptional regulators in *human* cells. The breadth of the claims exacerbate the complexity of the invention in that the claims encompass the use of non-human cells and the use of non-human Sp1 or B segment-binding B_3-AR *trans*-activating factors in an assay to determine the effects of a test compound on human cells comprising Sp1 and/or B segment-binding B_3-AR *trans*-activating factors. Thus, there must be some degree of correlation between the non-human analogs of the human Sp1 or B segment-binding B_3-AR *trans*-activating

factors and their function in non-human cells and that of the human proteins in human cells. The guidance and working examples in the specification are directed solely to the human proteins and assays done in human cells. There is no evidence of record in the instant specification or prior art that one can reliably extrapolate from results in non-human cells using the non-human analogs of the human Sp1 and B segment-binding B_3-AR *trans*-activating factors, making the practice of the claimed methods with non-human proteins and/or cells inherently unpredictable. Given the lack of guidance in the instant specification and prior art as to the correlation between how the non-human and human B_3-AR *trans*-activating factors function in their respective cellular environments, one of skill in the art would first have to determine such correlation in order to reliably predict the affects on the human B_3-AR *trans*-activating system based upon results in non-human cells and/or with non-human Sp1 or B segment-binding B_3-AR *trans*-activating factors. Therefore, the instant specification is found to be enabling only for those embodiments where the methods are practiced with human cells and with human Sp1 or B segment-binding B_3-AR *trans*-activating factors.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is vague and indefinite in that the metes and bounds of the term "express at very low level B_3-AR" are unclear. **This rejection is maintained for reasons of record in**

Papers No. 10 and 12 and repeated herein. How much of the B_3-AR can be expressed by the cell for it to remain at a "very low level"? This concept is not defined clearly in the instant specification and should be deleted from the claim language.

Response to Arguments

Applicant's arguments filed in Paper No. 13 have been fully considered but they are not persuasive. The response essentially argues: 1) the instant specification teaches several cell types that express B_3-AR at "very low levels"; 2) the specification explains that the level of B_3-AR expression in these cells is very low relative to B_3-AR expressing cells; and 3) the specification points to prior art in which cells are described that produce B_3-AR at very low levels.

The phrase "at very low" levels is inherently subjective and applicants' explanations in the specification do not provide an objective standard for what is "very low" level expression of B_3-AR expression. Even the explanation that it is considered "relative" to cells known in the art to express B_3-AR do not put a quantifiable number on what will satisfy "very low" expression. Which cell type is to be considered as the standard? How much lower does it have to be to satisfy "very low" expression? These questions are not satisfactorily answered by applicants specification, arguments in the response or the prior art cited.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
June 29, 2003